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THE NEUROPSYCHOLOGY OF AGING AND DEMENTIA

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INTRODUCTION

Although the term 'dementia' was originally used to describe a change in intellectual functioning, research into the cognitive deficits in aging and dementia has focussed primarily on memory processes. Likewise, much biologically oriented research has been directed towards the role of the hippocampal system - known to be essential for memory formation - in dementia. However, many other cognitive, emotional and behavioral changes can be noted in both aging and dementia. It is the purpose of this chapter to evaluate the nature, extent and pattern of these deficits in order to compare aging and senile dementia. Modern neuropsychology which is, by definition, the science which relates cognitive, emotional, and behavioral aspects with the underlying cerebral substrate, may be able to provide information which is essential for a better understanding of the biological processes underlying aging and dementia. This chapter is concerned with a critical reevaluation of neuropsychological research performed during the last 30 years. A description will be given of the cognitive functions in 'normal' aging, and in dementia, and the chapter ends with a neuropsychological interpretation of the cerebral substrate involved. The reader is referred to others for more extensive reviews on the neuropsychology of aging (1,2,3), memory (4,5), dementia (6), and the clinical signs of senile dementia (7).

COGNITIVE FUNCTIONS IN NORMAL AGING

Intelligence.

The question whether intelligence decreases with age has been intensively studied during the last decades. However, despite many studies, in which a gradual decrease in intelligence test scores was found with age, the matter is still regarded with controversy (1,2). Traditionally, research into intelligence of aged (or demented) subjects has been performed according to the psychometric tradition, which uses standardised test batteries. An important parameter which has often been studied with the Wechsler Adult Intelligence Scale (WAIS), is the differential response on 'Verbal' versus 'Performal' subtests of this test battery. It has been demonstrated many times that the Verbal IQ (VIQ) does not decline to a significant degree until fairly old age in normal subjects whereas

the Performal IQ (PIQ) decreases more rapidly with age. This differential response gives rise to several possible interpretations. A suggestion which has often been made refers to speedfactors: The inferior performance on performal subtests of the WAIS might be due to a general slowness in the subjects studied, as these tests tend to be timed whereas the verbal subtests are not (1,6). However, slowing becomes less attractive as an explanation as scores on other Intelligence tests (such as the Mill Hill Vocabulary Scale and Progressive Matrices) are also depressed though these test are not timed (6). According to another explanation, the VIQ/PIQ discrepancy reflects the fact that the performance on visuo-constructive tasks determines the PIQ, indicating that a selective loss of visuo-constructive or (visuo-integrative) ability might underly the intellectual deterioration. The most probable interpretation however refers to the fact that the verbal subtests measure well-practiced and overlearned activities whereas the performal subtests measure the ability to deal with new tasks and the acquisition of new information. (1,2,6). The selective deficit of aging or dementing subjects on performal subtests of the WAIS may thus have to do with impaired memory or learning ability more than with anything else (6). In addition to speed, memory, verbal and perceptual factors, a factor called 'General Ability' is an important determinant for the performance on intelligence tests. This indicates that educational level is important for the IQ score found, and explains the finding that the correlation between chronological age and intelligence is rarely as high as .50. (2)

It is clear that studies on intellectual functioning in aged/demented subjects has created more problems than it has solved. More relevant information has been obtained in studies in which specific cognitive functions such as memory are investigated.

Memory

As memory complaints are among the most frequently reported signs of decreasing abilities in both normal aged and dementing subjects, an enormous amount of research has been directed at establishing the nature of underlying memory disorders. Generally, different kinds of memory and memory disorder have been characterised (for a recent review on the neuropsychology of memory and the terms in common use, see 5). Information which has been acquired many years ago is described in the clinic by the term 'Remote Memory'. 'Recent Memory', on the other hand, is used to describe information which has been acquired some months, weeks, or only days ago. In the sixties, much research has been centered around the concepts of 'Short Term Memory' or 'Long Term Memory',

whereas a newer trend in memory research asks the question 'How information is processed and used'.

The essence of an information processing type of theory states that information from the environment is sensed by the sensory registers (visual, auditory, tactile, etc.) and passed onto a central processing unit. There is temporary storage in shortterm memory (primary memory), and the information is then transferred to longterm storage (secondary memory or longterm memory) by the process of 'Memory Consolidation'. 'Retrieval' from longterm storage can make the information available again. The most recent trends in memory research refer to the importance of the strategies which subjects use to consolidate and retrieve information (encoding processes, rehearsal, use of mnemonic aids, active search, etcetera). All these different aspects of memory have been investigated in relation to aging and dementia (see 4):

Recall and recognition memory. The question whether normal aging is characterised by a more or less specific deficit in consolidation and or retrieval has been approached experimentally as follows: The subject is required either to recall (actively) what he has learned in a learning trial, or he is asked to recognise (passively) the memorised information among several alternatives. The results obtained in this type of experiments is consistent, in that recall memory tends to fall with age, whereas recognition memory does not decrease to such a significant extent (e.g. 8). This has been interpreted in terms of a retrieval deficit in aging.

Sensory Memory. The first stage in informationprocessing which eventually gives rise to memory formation, is perceptual in nature. This first stage lasts several hundreds of milliseconds in healthy young subjects, in both the auditory modality ('echoic memory') and in the visual modality ('iconic memory'). According to Botwinnick (2) the studies reported until now suggest that elderly subjects have an impaired sensory memory: When very short stimulus durations were used (9) only 2 out of 10 aged subjects showed sensory memory whereas 9 out of 9 young adults showed it. With somewhat longer exposure duration (100 msec; 10) sensory memory was found in older adults but the extent was less than in younger adults.

Short term memory. (Primary memory). The second stage is also of a very temporary nature; it lasts several seconds and is conceived by some as a kind of 'working memory'. Short term memory is a temporary holding and organising process more than a structured memory store (4). According to Botwinnick (2) old and young are similar in short term memory as long as the number of items to be recalled is not greater than about four or five. However, in view of

the fact that some authors envisage short term memory to be a type of memory that can retain seven items plus or minus two (11), older people may be somewhat impaired when compared to younger subjects.

Long term memory. (secondary memory). An efficient consolidation into longterm memory requires some kind of organisation of the stimuli to be stored. Thus, the formation of new memories can be strengthened by rehearsal, mnemonic aids, imagery and other coding strategies, and it is especially the use of strategies which seems to be impaired in the aged (4). It is a general finding that elderly people are inferior in tasks involving acquisition and retrieval of new information. More specifically, some investigators found that aged subjects do not use strategies spontaneously, even when the experimenter presents such a strategy (3,4). It is only under some circumstances that the subjects can be encouraged to do so (12). These findings indicate that old people may be less able to (actively) manipulate and organise the content of short term memory (4); there is an age-associated deficit in the use of cues which are important for both encoding (consolidation) and retrieval processes. These findings can also explain the fact that the aged are characterised by inferior recall memory and relatively normal recognition memory, as the active use of strategies is not essential for a normal performance on recognition memory.

An important parameter with respect to the formation of stable memories refers to the speed with which the information is presented and/or reproduced. When the rate at which words in a word learning test were presented is high, old subjects performed less well than younger subjects, and this age-associated deficit was also present when the time to respond was low. When the time limits were not so strict, no age-associated deficits were found (13,14).

Another parameter which has been studied in relation to aging is the susceptibility to interference: Some studies claim that older people are inferior to younger subjects, but others conclude that no such age differences exist (4).

Problem solving.

As indicated above, memory and general ability are an important determinant for performance on intelligence tests (1,2), and especially on those subtests which measure aspects of problem solving ability. The inferior performance of elderly people on these tasks has been interpreted in several ways. For instance, several studies have attributed the difficulties to 'inflexibility'. This was defined in terms of 'giving up a selection procedure that once was effective but no longer is' (15), or the 'inability to shift concepts' (16). Others have shown that elderly people, generally, are less able to discern

relevant from irrelevant information: A redundancy of irrelevant information was found to be disruptive to the problem solving behavior (13). In addition, there was less efficient use of environmental cues for an optimal plan of action. For instance, when asking for extra information regarding the problem to be solved, old subjects performed in a more haphazard fashion. Likewise there was a lack of order in their informationseeking (see 2, for references). Characteristically, they did not have explicit knowledge of their goal until very late (17). Interestingly, certain personality characteristics which are often found in, and attributed to aged people, can be interpreted in terms of inflexibility, decreased concept shift and impaired ability to use (new) environmental information. This applies especially to trends towards intraversion, conservatism and cautiousness, and to the reluctance in making decisions, especially when the outcome is uncertain (2).

It will be clear that an inferior performance of elderly people on *complex* test of memory, perception and other cognitive functions can be attributed to difficulties in problem solving ability, unless care is taken that test-instructions and procedure are really understood by the subject. Neuropsychologically, the deficits described (inflexibility, difficulty with concept shifts, deficient use of environmental information to guide one's own behavior) are indicative of a primary deficit in the planning, control and evaluation of the behavior, and thus of frontal cortex involvement (18,19). For, the frontal neocortex monitors and programs activity of the whole cortex and creates the necessary conditions for the integration of environmental information with memories, to make an optimal action plan and to monitor its outcome (see later paragraphs).

Perception.

As discussed under 'problem solving behavior', the aged seem characterised by inflexibility and cautiousness, which may be interpreted in terms of a relative importance of old information over new information. Interestingly, perception in the aged seems characterised by a similar persistence of old information. Several experimental paradigms have been used and the results, generally, point in the same direction. The effect of a sensory stimulation persists longer in the CNS of the old subject, which makes the old subject more refractory or less able to respond to subsequent stimulation. This theory evolved from experiments which started in the forties, with the so-called 'Critical Flicker Fusion' technique: A brief (e.g. 20 milliseconds) light stimulus is presented, followed by others which are separated by a similarly brief time interval: When this time interval is progressively shortened, there

comes a moment that the viewer sees one steady light. The sequence of light stimuli is then 'fused'. Old people experience fusion with longer inter-stimulus intervals. This indicates that the first stimuli are *perceived* for a longer period of time after discontinuation of the physical stimulus (e.g. 20, see 2). Similar findings were done with sounds and tactile stimulus (see 2, for references).

Other studies in favor of the stimulus persistence theory either used the technique of 'backward masking' or that of 'stimulus enhancement': Two (different) stimuli are presented, separated by a short time period. When the second stimulus is a potentially masking stimulus, older people are inferior in the recall of the first stimulus (e.g. 21). When the second stimulus is a potentially 'enhancing' stimulus (that is, when it adds information which is missing in the first), the performance of old people was better than controls (22). All the studies mentioned, are in line with the notion that the first stimulus is perceived for a longer time in older people. Similarly, visual aftereffects seem to be present for a longer time period in the old (23, and others). Neuropsychologically, a lack of inhibition of irrelevant information may underly this stimulus persistence.

Older subjects required more time to process visual input (24). Others found that elderly people are inferior in tasks in which parts of a complex visual figure have to be integrated to a meaningful whole. (25) In addition, figure-background discrimination is harder for the elderly than for the young (26).

In conclusion, aged people are inferior in tasks of simple and complex perception. This may partly be because stimuli, once perceived, are present for a longer period of time, partly because an efficient perception takes more time.

Motor performance.

The motor performance with which this section is concerned, does not depend on motor factors alone but on activities of a complex functional system, any part of which may limit performance in particular circumstances. In an information processing model, the flow of information may be envisaged to go via several discrete stages, such as 1. Sensation (level of the senses), 2. Perception (within CNS), 3. Translation from perception to action (CNS), 4. Effector control (CNS), 5. Motor output (level of peripheral nerves and muscles). (7) Stages 3 and 4 refer to the integration of information from the senses, the generation of plans to use this information for an act, and the computation of the motor performance. This planning is a prerequisite in order to perform the planned action in a sequential order (18,19).

Welford (27) in a review of literature data and own research over the past 30 years concluded that the main limitations in motor performance which elderly people experience seem due to a combination of a reduced speed, and less efficient information processing in stages 3 and 4. He concluded that aged subjects are considerably slower in performing relatively large movements at maximum speed. This seems primarily due to peripheral (e.g. muscular) limitations. Most other movements are not limited by muscular factors but by the speed of the decisions that have to be made to guide movements. When decisions can be made beforehand, such as in simple reaction time tasks, and in simple repetitive movements, the change with age is relatively small. The performance on a new or complex task however, is much slower; the extra time is needed for the planning of the (stages of) the motoract. In addition, elderly people pay more attention (and thus more time) to the signals presented, before they act. This is especially the case when the relation between signal and response is not straightforward. The performance of older people becomes slower and less accurate when the subject has to choose between alternatives or when an extra judgement of spatial relations has to be made (see 27). Clearly, such a complex motor task has the characteristics of a problem solving task as discussed above.

Thus, the performance on simple tasks which do not require a complex 'computation' of the motoract is relatively normal in aged people. The performance in complex motor tasks and in tasks requiring complex sensorimotor integration, is inferior because of more time needed for decisionmaking and planning of the movement to be performed. This is, once again, an indication for a planning deficit more than a deficit in motor performance per se.

Discussion.

In reviewing all the studies on cognitive changes in the elderly, it is readily apparent that there is an age-associated decrease in performance in virtually all the cognitive functions which are tested: The aged are characterised by a deterioration in intellectual functioning, memory, language functions, problem solving and perception, and it seems that there are specific parameters which are involved more than others. For instance, elderly people are not inferior in tasks in which they can rely on well established skills and knowledge, whereas they perform poorly in tasks involving new information, especially in situations in which the planning of new activities or the active use of coding strategies in recent memory is important. In addition, trends towards inflexibility, cautiousness and conservatism are found, which are paralleled by 'stimulus persistence'. The speed of information processing

seems to decrease, but more information has yet to be gathered on this subject.

Taken together, the data obtained, are not consistent with the notion that a relatively isolated memory deficit ('benign senescent forgetfulness') is the only, or major cognitive change associated with aging. The dementia research gives rise to a similar picture:

CLINICAL SIGNS OF DEMENTIA

This paragraph is concerned with a brief description of the clinical syndrome of senile dementia. This description will be given, in order to compare the cognitive deficits found in aged subjects to those which have been demonstrated in demented, and which will be evaluated in a later paragraph. The description is based on an account by Strub and Black (7). These authors described the symptomatology of patients suffering from primary degenerative dementia with an emphasis on the diagnosis 'senile dementia of the Alzheimer type'. Although similarities exist with other dementia's (e.g. Pick's disease, multi infarct dementia), differences exist as well. Pick's disease, for instance is characterised by more 'frontal lobe signs' than Alzheimer patients. In addition, although these dementias have a fairly characteristic mode of presentation, there is considerable variation within each group.

Generally, demented people are not especially characterised by memory deficits, but also by intellectual deterioration, and changes in affect, personality and social functioning. The symptoms develop in time, intensity and diversity. Alzheimer's disease can occur at any age, and the course of the illness is also variable: Some patients live only a few months after the initial assessment, but 25-30% of the patients live over 10 years, and some live over 20 years (28). The average life span from diagnosis to death is slightly over seven years (29).

Generally, the patient suffering from primary degenerative dementia goes through a number of successive stages, through which a fairly clear 'evolution' or temporal sequence of symptoms is evident (7).

Stage 1. Changes in social behavior and in expressed emotions are among the early signs of primary degenerative dementia. There is a lack of normal initiative and interest in family, work and other activities. Increased fatigue and restlessness are frequently noted in this stage, as well as depression and anxiety. Some patients are overly concerned with somatic complaints whereas others deny any problem. There is often an accentuation of previous personality traits superimposed upon a background of euphoria or apathy. In other patients, personality changes are noted which are quite

uncharacteristic of the premorbid personality (e.g. inappropriate or bizarre behavior). This applies especially to patients with extensive frontal lobe lesions such as those suffering from Pick's disease, Huntingdon's chorea or general paresis.

Cognitive changes such as memory deficits are the most frequently noted early signs of the disease process. The patient forgets names and recent events, and experiences increasing trouble in finding things around the house. Recent memory seems to be affected more than remote memory. In addition to memory, general problem solving ability deteriorates; this is most evident in new tasks in which the patient can not rely upon well established skills and routines. Furthermore, comprehension and the expression of complex ideas, abstract thinking and critical judgement deteriorate. More basic cognitive deficits also become evident, such as an impaired visuo-motor integrative ability. A routine neurological examination is usually normal in this stage.

Stage 2. The signs noted in stage 1 accentuate. The patient is less able to manage his personal and business affairs, because of failing memory and lack of initiative. Several language problems also become evident although they do not yet reach the level of clearcut aphasia: Speech remains fluent at first, but circumlocutions and paraphasias appear, and the patient experiences difficulties in word finding. The ability to express abstract thoughts decreases and there is an overall decrease in intellectual functioning. The restlessness already noted in stage 1 increases; patients become upset at night, and they tend to wonder about. They may constantly be manipulating things in their hands. Emotionally, patients in this stage often retain sufficient insight into their condition to develop secondary anxiety and depression; the dementia may thus appear more severe than it is.

Stage 3. With further progression, the patients develop a clear aphasia, apraxia and agnosia. Spontaneous speech decreases further; there is a tendency to echo what is said (echolalia), there is greatly reduced comprehension and an inability to name objects. This anomia appears to be more than a simple problem in finding the correct word: the patient characteristically acts as if not recognising the object and the failure therefore is a visual agnosia. An ideomotor apraxia develops, i.e. a difficulty with the execution of previously learned skilled movements, such as combing the hair. In addition, a so-called ideational apraxia develops, which is a total disruption in the ability to carry out a complex action composed of several relatively independent acts (such as taking a match from a box and lighting a cigarette). Inattention and distractibility become very common in this stage, as well as involuntary

emotional outbursts. A number of primitive/infantile reflexes reappear and are now evident from the neurological investigation. In addition, involuntary movements are noted, and urinary and fecal incontinence begins. In short, the patient experiences increasing difficulty in inhibiting natural reflexes. In some patients features of organic psychosis are prominent.

Terminal stage. The patient becomes uncommunicative, uttering only short phrases of undirected babbling. Emotions are involuntary, delusions appear and the patient finally gets completely apathetic and withdrawn. More neurological signs become apparent, including generalised seizures (in 22% of the patients during the last year of life (29)). Death usually results from pneumonia, aspiration or urinary infection.

Discussion.

Several important points emerge from the foregoing. When a patient suffering from primary degenerative dementia is followed through an appreciable time period, a progression of symptoms is seen which seems to follow a more or less clearcut sequence. The sequence emerging in senile dementia of Alzheimer's type is different from that noted in Pick's disease although the terminal stages may be similar (Strub and Black 6,7). Careful examination of the mental status of the patient is therefore very important for an early diagnosis of dementia (of whatever etiology), as neurological signs develop only in the terminal stages. An extensive neuropsychological evaluation may therefore be the only means for an early diagnosis.

In view of this temporal sequence in the development of symptoms, there is quite some variation within the demented group: Of course patients in the first stages differ in quantitative and qualitative ways from those in the later stages. Besides, there is quite considerable variation due to personality characteristics, as premorbid personality tends to be exaggerated in the first stages. This may explain an important part of the individual differences within a group of patients that may be pathogenetically homogenous. With respect to the stages proposed by Strub and Black (7): Others differentiate between 'mild', 'moderate' and 'severe' dementia, although the criteria used for the inclusion of a patient in the different groups are usually vague. This may be an important reason for the difficulty in comparing different studies with dementing patients. Of course, the differentiation between different types of dementia is of utmost importance for treatment and management of the patient at home or in a nursing home, but also for the assessment whether the memory complaints may indicate a relatively 'normal' senescent forgetfulness or are the early sign of beginning dementia. With respect to the differentiation

between senile dementia of Alzheimer's type and Pick's disease, the latter are generally characterised by neuropsychological signs of frontal lobe dysfunction (such as inappropriate social behavior and bizarre behavior) without clearcut intellectual deterioration or memory impairments. In addition, a differentiation with dementias of a vascular origin can usually be made upon a careful examination of the pattern of cognitive deficits. For instance, a patient who has difficulty in object naming (anomia) without a concomitant impairment in object recognition, or apraxia may be suffering from more localised cerebral dysfunctions, such as based on cerebral vascular insufficiency in the left temporo-parietal region. A problem in this type of interpretation is due to the fact that in primary degenerative dementia multiple small infarctions may accompany the degeneration of cortical tissue, such that the cognitive dysfunctions which are evident in a particular patient may result from both the infarctions and neuronal degeneration (7).

With respect to the assessment of specific deficits in the different groups of demented patients, some indications exist that indeed such differences can be objectively assessed: We have done an extensive neuropsychological investigation on a heterogenous group of patients suspected of senile dementia, to assess whether the different subgroups of patients show any specific pattern of cognitive deficits (30). It turned out that the dementing patients as a group were inferior to younger patients suffering from a traumatic head injury in almost any task. The demented group as such was characterized by large individual variation (30).

Interestingly, patients coming from a psychiatric setting appeared to differ considerably from those coming from the neurological clinic. In a preliminary investigation, which was designed to compare both groups with respect to their neuropsychological test profile (J. Jolles, unpublished) the psychiatric patients were characterised by planning disorders, perseverative tendencies, lack of inhibition and other deficits which are indicative of frontal neocortex dysfunctions (18, 19). Those cognitive functions which depend on a proper functioning of posterior neocortex areas were relatively well preserved. The reverse was true for the neurological patients suspected of dementia. These patients did not manifest clear frontal lobe signs, apart from an inferior planning function. Their deficits were in the realm of complex visuo-constructive tasks, complex language functions and higher intellectual functioning (J. Jolles, unpublished). These deficits, according to Luria (18,19) are suggestive of dysfunctions in posterior neocortex areas. These data suggest that the discrimination between different subgroups of dementing patients is

in principle possible on the basis of an extensive neuropsychological investigation. Furthermore, the pattern of deficits of the psychiatric group could be suggestive of an early manifestation of Pick's disease. However, this disease is not very common; this could indicate that either the signs of dementia which are manifested by our psychiatric group have another origin, or Pick's disease is disguised as a 'functional' psychiatric illness. We are presently performing a more thorough investigation to elucidate this point. Generally, the question of the specific cerebral substrate which underlies the cognitive dysfunctions is of importance in view of the data from biologically oriented research which points to the involvement of cholinergic fibres projecting to the neocortex (see last paragraph).

THE NATURE OF COGNITIVE DEFICITS IN SENILE DEMENTIA.

Intelligence.

As the term 'dementia' implies a disturbance in cognitive functioning, many studies have addressed themselves to the determination of intellectual deficits in dementing subjects. As was evident from the foregoing discussion, intellectual changes become evident in the course of the illness. These clinical observations have been objectified in experimental studies, in that demented patients show a lowered mean IQ (31). Unfortunately, the research which has been performed with respect to the differential performance on 'verbal' versus 'performal' subtests of the WAIS has not yielded clear insights into the cognitive functions underlying the intellectual deterioration of dementing patients. The interpretational problems are similar to those encountered in the study of intellectual functioning in normal aged subjects (see second paragraph and 6). Thus, the performal IQ of demented is much more depressed than the verbal IQ, but it is not easy to characterise the underlying deficit as being due to general slowness, failing memory or problemsolving ability, or other factors (6). Those authors who conceive of dementia as a disease process in which 'crystallised intelligence' (abilities which are well practised and overlearned) is relatively more preserved than 'fluid intelligence' (new activities which do not rely upon familiar or routine strategies), simply rephrase the findings in other terms and thus add little to our knowledge of what is happening in dementia (6). The findings done until now do not indicate that there is more than a quantitative difference between normal aging and senile dementia.

Memory.

Memory processes are extensively studied in demented patients according to the same line of thinking as indicated above for aging research. It has been

the aim to define some stage in which demented patients might be specifically impaired. Most of the research which has been carried out, concerned the distinction between short term memory and long term memory. It is only recently, with the advent of informationprocessing theories, that other stages such as sensory memory have also been investigated:

Sensory memory. There seems not to have been much research on sensory memory in demented, possibly because these experiments are difficult to conduct with these patients (6). There is one preliminary study in which the 'backward masking paradigm' was used (see second paragraph), to measure iconic memory. Demented patients were inferior to controls in reporting the first stimulus, which indicates that masking had occurred. According to the authors (32) this could be due to a defect in attention or iconic memory, and/or an enhanced susceptibility to interference. According to the theory on stimulus persistence, there may have been a lack of inhibition of the first percept.

Short term memory. Inglis (33,34) found that elderly psychiatric patients were slow to learn paired associates. There was an inferior performance in both recall and recognition, which is suggestive for a problem in acquisition rather than in retention. Later experiments favoured the hypothesis that short term memory does not function properly (35, but see 6). Experiments in which a wordlist has to be learned give some clue as to the differential involvement of short term and long term memory: Characteristically, the first and the last words of such a list are learned better than words in the middle of the list. The better retention of the last words in the list is ascribed to the fact that these words are still in short term memory, while the superior remembrance of the first words is ascribed to the fact that these are already transferred to long term memory. Characteristically, demented patients do not show a better retention of the first and last words of this list. This finding may be taken to indicate that demented experience both a short term- and a long term memory deficit.

Of course, the long term memory deficit could be secondary to the impairment in short term memory. This hypothesis has been tested by Miller (36). He presented the words in the list at a reduced rate, and found that control subjects performed better in this condition, as indicated by the number of words recalled from the beginning of the list. The demented patients did not benefit from the reduced presentation rate. The interpretation was that the patients could not use the opportunity to increase the consolidation of short term into long term memory, indicating that the memory impairment in dementia has at least two components (involving STM and LTM). The notion that long term

memory is involved was supported by the finding that demented subjects have appreciable difficulty in learning word lists which are longer than the memory span (i.e. the number of words that can be correctly recalled after a single presentation). Long term memory is essential for this supra-span learning (37).

Several interpretations are given to the performance deficits discussed. Apart from the possible involvement of 'real' memory processes, the impairments could be a secondary consequence of an attentional deficit or impaired sensory memory. Furthermore, a decreased ability in the use of coding strategies is also probable: There is support for this notion in view of reduced efficiency with which material was acoustically coded by demented patients (38).

Long term memory. Word list learning experiments are also used for the measurement of long term memory. Experimentally, recall and/or recognition are tested after an interval in which distraction prevents the subject from rehearsal of the words.

It has appeared that demented patients perform bad in the delayed recall and -recognition condition (39). However, the patients were indistinguishable from controls in a 'partial information' condition in which the subjects were given the initial letters of the words as a cue (39). Similar findings have been done with patients suffering from the amnesic syndrome (40), and the data may indicate that some trace has been formed which is too weak to get expressed unless extra cues are given which enhance it. Such an interpretation suggests that in addition to an improper memory consolidation (resulting in weak traces, retrieval is also inferior in demented subjects. Again, this may be due to a decreased or inefficient use of coding strategies (second paragraph). Work in progress fails to indicate a clear difference between aged and demented subjects in this respect (6), but it is known that both groups of subjects perform worse than younger controls (see also second paragraph). An alternative explanation for the partial information effect was given by Warrington and Weiskrantz (40): Successful performance would depend not only on the ability to recall the correct words but also on the ability to inhibit the recall of incorrect words. However, Miller and coworkers (41) tested this 'disinhibition hypothesis' and found no support for it. They did find however that demented subjects became progressively less able to recognise a correct word from several alternatives as the number of alternatives increases: That the choice between alternatives is difficult for these patients was also found in an experiment in which a single choice (yes/no) was compared to a forced choice between yes and no (two alternatives). The forced choice appeared to lead to better performance (42), possibly because a response is elicited also when the patient

is insecure. The personality characteristic '(over)cautiousness' may prevent the elderly/demented subject from responding in other choice situations. In other words, the elderly subject has a 'negative response bias'; he prefers to choose 'no' unless he is really sure that the answer has to be different. Taken together, the memory studies indicate that demented people are inferior in several aspects of memory, especially relating to the acquisition of new information. (sensory memory, short term memory and long term memory; recent memory). With respect to remote memory, the issue is less clear. The commonly held belief that old people have a good preservation of remote memory may not be right. Careful clinical observations suggest that some 'childhood memories' can become dominant at the cost of other memories and this is indicated by many gaps in remote memory. More systematic studies of remote memory have to our knowledge, not been performed.

Language and other cognitive functions.

Language. As already noted in the description of clinical signs of dementia (third paragraph), discrete language problems appear fairly early in the disease process. In later stages, a clearcut aphasia develops. Ernst et al. (43) showed that the only feature which all their dementing subjects seemed to have in common was a general poverty of vocabulary in narrative speech, but many dementing subjects showed impairments in object naming. In other studies, age-matched controls also showed a relative impairment in naming, although demented subjects were clearly inferior in this respect (44,45). Demonstration of the use of the object improved naming in the demented but had no effect in the control subjects (44,45). This may indicate that the demented patients do not recognise the object in addition to not being able to find the correct word. Patients which are aphasic due to a focal lesion also have a deficit in object naming but the aphasic, in contrast to the demented patient characteristically gives the strong impression that he knows what the object is but he just cannot find the right word to describe it (46). In experiments designed to assess word production in demented subjects, Miller (47) used a fluency task in which the subjects were required to produce words beginning with a predefined letter. It appeared that the demented subjects produced less words in a 5 min period than controls, but demented patients did not rely on a small set of commonly used words as might have been expected. In other words, the data are not consistent with the hypothesis that the pattern of word use is different in aged versus demented people.

In addition to the general poverty of speech and the naming difficulty, demented subjects showed repetitive elements in their speech. This repetitiveness may

be a type of perseveration stemming from linking a word inappropriately to an object when the same word had been linked appropriately just before (2). Such a perseveration, again, may be an aspect of frontal cortex involvement (19,20).

Other cognitive functions. Some perceptual deficits have been demonstrated in demented patients (48). Visuospatial functions are inferior, whereas visuoconstructive tasks in which the patient is required to copy drawings are among the tests frequently used in the assessment of dementing patients (7). Patients with senile dementia seem to have appreciable difficulty in solving paper and pencil mazes; they also have an impaired appreciation of reflected space (such as a mirrorview). Dements may also experience a disintegration of the body schema and they are impaired in tasks requiring the subjects to fit together pictures of different parts of the human body to make a whole (for references, see 6).

Some experimental data exist which substantiate the clinical impression that demented patients are distractible (49), but there is an obvious need for further research. The same applies for studies on other parameters such as informationprocessing. In one study which addressed this question (50), it was found that the dements were inferior to age-matched controls. Another finding in informationprocessing research concerned an experiment on speed of movement: It appeared that dements were slow partly because they were slower to decide when and where to move (31). Clearly, this finding of an impairment in decisionmaking and in speed supports similar findings which were done in other experimental paradigms (see above).

AGING AND DEMENTIA RESEARCH: SOME METHODOLOGICAL ISSUES.

In reviewing studies on aging and dementia one is struck by important differences between the studies, with respect to the characteristics of the patient population described. Some studies do not clearly discern primary degenerative dementia from dementias of other origin. Furthermore, the progress of the disease (the stage) is often not described, which makes the comparison of different studies difficult, if at all possible. This indicates that future research in this field may benefit from a careful clinical diagnosis of the patients involved, and from the use of standardised classification systems such as DSM-III (51). In addition, control groups of age-matched or control subjects should also be assessed carefully, especially in view of differences in personality characteristics, which tend to confuse age-associated cognitive changes: For instance, some people over 65 years of age do not retire and remain active

until high age. Other elderly people disengage; either because they want to, or because society isolates them. These social and personality factors will have a profound influence on psychological (coping) mechanisms and the social relations of these subjects, and thus on their cognitive functioning. In addition to the factors mentioned, the studies reviewed differ with respect to the age of the subjects: the brain of a dementing subject aged 85 in stage 2 can be expected to differ from that of a similar patient, aged 65!

A similar point can be made, concerning the design used to compare the groups (2). This point is of importance, as crosssectional research designs tend to exaggerate agedifferences (due to differences in education level and vocation), while longitudinal research tends to underestimate agedifferences (2). A related problem concerns the fact that older agegroups can be expected to contain a selection of the most healthy subjects of the original group; the remaining part of this group will be either demented or dead by that time.

The notion that some type of selectionprocess acts to change the composition of different agegroups can be illustrated by research performed in our institute (J. Jolles, unpublished data; fig. 1).

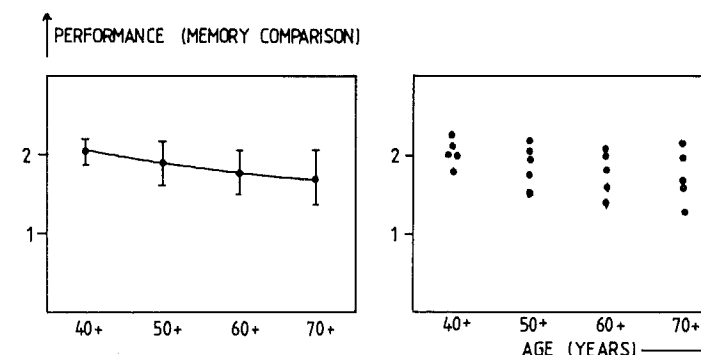


Fig. 1. Rate of informationprocessing as a function of aging.

Subjects of different age were subjected to an informationprocessing task based upon the memory comparison task of Sternberg (see 30). There were 5 subjects per age group. The intercept of the reactiontime versus memoryset size function was taken as ordinate in the figure (performance; arbitrary units). The left figure gives mean \pm s.e.m. for the four agegroups. The right figure gives the raw data for the twenty subjects.

Healthy volunteers of different ages were subjected to an information processing task based on the additive factor method of Sternberg (52). As shown in the figure, there is a gradual increase in mean 'rate of information processing' with age. However, group means appear to give a wrong impression of the relation between performance and age, as the variability within each age group increases. The number of individuals which are slower than normal increases with age, suggesting that there may not be a gradual decrease of performance with age, but rather a discontinuity which may be induced by a relatively small event such as a disease, or emotional events. These findings suggest that it is important to look with caution at studies in which the performance decreases gradually with age.

THE NEUROPSYCHOLOGY OF AGING AND DEMENTIA.

Neuropsychological research in aging and dementia has primarily focussed on memory processes although it is very clear that other cognitive functions are impaired as well. The quantity of research work on memory may thus give the wrong impression that memory is the major function involved. There is an obvious need for further studies of information processing, language, perception and planning/organisation/coding processes. There is a parallel in biological research of aging and dementia, in which the focus is on the structure and function of the hippocampus (which is involved in memory function, see 53). The emphasis on memory and hippocampus tends to obscure the fact that other cognitive functions (information processing, language, perception, problem solving) and other brain areas (other neocortical and limbic/subcortical) are involved as well. The neuropsychological knowledge discussed so far does not give any indication that there is more than a gradual difference between 'normal' aging and primary degenerative dementia (Alzheimer type). Of course, when demented patients are compared to age-matched control, the demented perform worse on all the test parameters measured. But, generally, there is not a different *pattern* of cognitive deficits in aged and senile demented subjects. Thus, as pointed out in the preceding paragraphs, a relative deficit is seen in the areas of intelligence, language functions, memory, problem solving, perception, coding processes etcetera. This indicates that -on the basis of neuropsychological data alone- senile dementia might be considered 'exaggerated aging'. It is important to note that this issue is a controversial one. Several authors have a similar view on the basis of (neuro)biological data (e.g. 54) whereas others state that the cerebral processes underlying 'normal' aging are different from those underlying senile dementia (this volume).

Another point to make, concerns the use of neuropsychological- and other tests for the behavioral assessment in senile dementia. It may not be very relevant to show that demented perform worse than controls: We must not step back to the fifties, when it was considered important to discern 'functional' from 'organic' disorders by the use of tests. It is presently more relevant to investigate the pattern of impaired *and* unimpaired cognitive functions. Similarly, knowledge of changes in performance under different (task- and environmental) conditions may give information which is relevant for patient management and wellbeing, as the impaired performance of the dementing subject may be maximised by a proper selection of the optimal stimulus configuration and environmental conditions. Apart from providing hints which are of practical relevance in patient care, modern neuropsychology may be able to provide insights with respect to the cerebral substrate involved in (aging and) senile dementia. After all, neuropsychology is the study of brain-behavior relationships and, in principle, may provide the bridge over the gap which separates several disciplines such as psychology, neurology, chemistry and biology (53). A potential theoretical contribution, for instance, concerns the localisation of the cerebral substrate involved. The nature of the memory disorders which are associated with aging and dementia suggest that limbic/subcortical structures are involved (especially those involving the hippocampus; this notion evolves from the consideration that the memory deficits are modality aspecific, and that there seems to be an impairment in the consolidation of new information). However, another important aspect of memory processes which is frequently overlooked, concerns the impairment in encoding processes; the search in memory is less effective, with a consequent impairment in active recall (with preservation of passive recognition); there is also less efficient planning and programming. These cognitive deficits in both aged and demented patients suggest that frontal neocortical structures may be involved. Likewise, deficits in other cognitive functions are in line with this notion, e.g. the (relative) lack of inhibition, the stimulus persistence, lack of flexibility, deficits in planning (problem solving behavior) and others. In fact, all the data which have been gathered by clinical and experimental neuropsychological research are suggestive of frontal cortex dysfunctions: According to the theory of the eminent Russian neuropsychologist A.R. Luria (18,19), a distinction can be made in three types of frontal syndromes which are characterised by a different (frontal) localisation. As will be evident from table I, the associated cognitive deficits nicely describe the deficits which characterise both aging (very mild) and senile dementia: The dysfunctions

described in stages 1 and 2 (paragraph 2) resemble the signs of Luria's frontal syndromes of the medial and basal zones (type B and involvement of tertiary areas). In later stages, syndrome A (involvement of secondary cortical areas) may also become apparent (see table I).

TABLE I.

COGNITIVE DEFICITS ASSOCIATED WITH FRONTAL CORTEX DYSFUNCTIONS.

LOCALISATION	COGNITIVE, EMOTIONAL AND BEHAVIORAL DEFICITS
A. Lateral and mediobasal zones.	Disturbances in organisation and planning of the motor function: perseverative tendencies; general inertia; adynamic speech regulation.
B. Basal/orbital and medial zones (connected to limbic system and reticular formation).	Disruption in emotional control; impulsivity; disinhibition of all activity.
C. Medial zone (part of the lower structures of limbic system).	Memory disturbances; confabulation tendencies; disturbance in orientation; lack of flexibility in thinking and decreased shifting from one conceptual frame of reference to another.

The table is based upon Luria (1966, 1973, 1980).

Parallel with the development of symptoms involving the tertiary (association) areas of the anterior (frontal) neocortex (type B and C), similar observations can be done with respect to cognitive functions which depend on proper functioning of the tertiary areas in the posterior neocortex. For instance, the higher-order integration between sensory modalities breaks down earlier than the cognitive functions which depend on secondary areas (e.g. language functions, figure background discrimination) or the primary projection areas. In fact, the temporal sequence of the development of cognitive deficits in senile dementia (Alzheimer type) suggests that there is a gradual increase in the number of neocortical areas involved, the tertiary areas degenerating

before the secondary areas and the primary areas staying relatively intact until very late in the disease process: This appears from the fact that the performance of simple motor acts is preserved (activity of the primary motor cortex) as is the use of syllables and phonemes (but not words) in indirected babbling, which severely demented patients are still capable of. Support for this view comes also from histological investigations in which it was found that several cortical areas are indeed relatively spared in the course of this disease (e.g. 55,56). In addition, it has been known for some time that there is a correlation between extent of cortical degeneration (senile plaques) and poor test performance (e.g. 57). Interestingly, when the notion that tertiary, secondary and primary cortical areas degenerate in that order, is true, this degeneration is exactly the reverse of the development in ontogenesis (primary projection areas develop before secondary, and these before tertiary areas: This is known as the 'law of the hierarchical structure of the cortical zones', 18,19). This would suggest that the processes underlying aging and dementia are the reverse of those in ontogenesis. Further research should be addressed at elucidating this interesting possibility. A final point to be discussed, concerns the question "What are the *very* first signs of decreasing abilities in aging and dementia?. What happens before the clinical stage 1?". In our opinion, the neuropsychological data suggest that the very first symptoms depend on dysfunction of ascending fibres to the neocortex (the 'Block I' of Luria 19,20) and of fronto-limbic connections. On the basis of neuropsychological knowledge alone, one is tempted to hypothesize that the cognitive deficits associated with neocortical degeneration are *secondary* to dysfunctions in the subcortical fibre systems. As is clear from the biologically-oriented research on the involvement of cholinergic and monoaminergic fibres, a primary deficit in primary degenerative dementia may indeed be the subcortical degeneration of these fibres (e.g. in the Nucleus basalis of Meynert, or in the Locus Coeruleus; for a review see this volume and 58). This results in a secondary degeneration of the cortical areas, which were once innervated by these ascending fibres. This interesting possibility should be investigated more intensely. We are presently performing neuropsychological research in patients suspected of very early beginning dementia with the hope of thereby establishing the essence of the early signs; Our emphasis is on informationsprocessing tasks, and especially on the speed of informationsprocessing; this focus is based upon the hypothesis that decreased speed is the characteristic deficit associated with dysfunction of ascending fibre systems (18,19).

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DISEASES OF THE AGED